

FREQUENCY OF CULTURE-NEGATIVE NEUTROCYTIC ASCITES IN CHRONIC LIVER DISEASE PATIENTS PRESENTING TO TERTIARY CARE HOSPITAL, PESHAWAR, PAKISTAN

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ABSTRACT

There is increased morbidity and mortality in cirrhotic patient having ascitic fluid infection. There are two types of ascitic fluid infection i.e. spontaneous bacterial peritonitis (SBP) and culture negative neutrocytic ascites (CNNA). By definition, in Culture-negative neutrocytic ascites (CNNA) polymorphonuclear cells count is more than or equal to 250/mm³ with negative results of ascitic fluid culture and absence of any intra-abdominal source of infection. Secondary causes like pancreatitis, peritoneal carcinomatosis, tuberculous peritonitis etc should be excluded. CNNA is a type of ascitic fluid infection which was first described in 1984. It has been shown that SBP has same prognostic, clinical and therapeutic characteristics. However it has been shown that CNNA has lower mortality as compared to spontaneous bacterial peritonitis. Third generation cephalosporin is considered to be the most effective drug in treating SBP. The following criteria is used for the diagnosis of CNNA (1) neutrophil count more than 250/mm³ (2) culture negative ascetic fluid (3) lack of any intra-abdominal infection (4) no antibiotic received in the last one month (5) no clinical evidence of pancreatitis. Due to increased mortality it is suggested to treat CNNA with antibiotic as early as possible. A descriptive cross sectional study was conducted on CLD patients admitted with ascites in Lady Reading Hospital, Medical Teaching Institutions, Department of Gastroenterology, from 1st September 2011 to 31st August 2016. The aim of our study is to determine the frequency of CNNA in patient of chronic liver disease presenting to tertiary care hospital. The cause of cirrhosis in most case was hepatitis C followed by hepatitis B etc. Most patients were in Child-Pugh Class C stage. Sampling was done by non probability consecutive sampling technique. A total two hundred patients were enrolled in this study among which 120 were male and 80 female. Culture negative neutrocytic ascites was found in 118 (59%) patients. In the prevalence of CNNA, no considerable difference was found regarding age, sex and duration of CLD.

Conclusion: It is concluded that 59% (118 out of 200) of the patients with chronic liver disease and ascites presenting to tertiary care hospital have culture negative neutrocytic ascites.

Keywords: Culture-Negative Neutrocytic Ascites, Chronic Liver Disease, portal hypertension.

INTRODUCTION

Chronic liver disease progresses to cirrhosis of liver characterized by fibrosis, scarring and nodule formation. SBP is considered to be the foremost complication in cirrhotic patient.¹ Patients with cirrhosis are at high risk of developing many complications and have decreased survival.² Among the patients with CLD, the major complications include ascites, portosystemic encephalopathy, hepatorenal syndrome, hepatopulmonary syndrome, coagulopathy, SBP, hepatocellular carcinoma etc which are due to either portal hypertension, abnormal synthetic functions or both.³ Among the major complications of cirrhosis, ascites seems to be the most frequent one, along with hepatic encephalopathy and the hemorrhage caused by

the rupture of the esophageal varices.⁴ In patients with cirrhosis, the complication most frequently develops is ascites along with portosystemic encephalopathy and variceal bleed. These patients are increasingly susceptible to develop infections primarily due to poor defense mechanisms. The most common and serious complication is SBP followed by UTI, lower respiratory tract infections etc. There is still controversy in clinical importance and prognosis of CNNA in patient with cirrhosis. There should be Low threshold for SBP to be investigated and treatment should be instituted as early as possible without waiting for culture and sensitivity report but it is essential to take ascitic fluid for routine examination and culture and sensitivity testing in all cirrhotic patients with clinical impression

of spontaneous bacterial peritonitis before commencing treatment because of evolving resistance due to injudicious use of antibiotics, *E. coli* and *Klebsiella* are the most common organism being reported to be implicated in causation of SBP and treatment should be directed against these organisms, however, after culture and sensitivity report, treatment must be tailored accordingly.

SBP was described in 1970, since that time SBP related mortality has significantly declined from 80% to 30% this is mainly due early diagnosis and immediate treatment.⁵ SBP is the infection of the ascitic fluid that occurs in the absence of a visceral perforation and in the absence of an intra abdominal inflammatory focus such as abscess, acute pancreatitis or cholecystitis. In patients with SBP it is of utmost importance to have one germ being isolated on C/S testing if positive.⁶⁻⁸ However polymicrobial infections on C/S testing would raise the suspicion of secondary peritonitis.⁹ CNNA is another type of ascitic fluid infection in which C/S test is negative but rest of the diagnostic criteria is same as for SBP and other causes of neutrocytic ascites (pancreatitis, peritonitis, tuberculosis and peritoneal carcinomatosis) must be excluded.¹⁰

METHODOLOGY

After approval from ethical committee of Medical Teaching Institution, Lady Reading Hospital Peshawar, 200 patients meeting inclusion criteria admitted at Gastroenterology and Hepatology unit MTI Lady Reading Hospital were included Patients admitted with clinical presentation of ascitic fluid infection and also those patients with asymptomatic infection were also included in the study. Data regarding patient age, sex, clinical presentation, complications as well as laboratory findings were collected and Child-Pugh Class was calculated. 200 patients with ascitic fluid infections fulfilling the criteria of SBP or CNNA were enrolled while patients who had non cirrhotic causes of ascites, secondary peritonitis / tuberculous peritonitis or malignancy or those who had received antibiotic within one month were excluded from the study. Diagnostic tap was done by sterile method on bed side using 20cc disposable syringe and the specimen was then put in EDTA tube and analyzed within 3 hours. The specimen was then centrifuged for 3 minutes in laboratory for total and differential count, total proteins. Gram staining and C/S testing of 10 ml ascitic fluid were also performed using aerobic and anaerobic culture bottles containing trypticase soy broth and then processed. At the same time blood was also taken in aerobic and anaerobic culture bottles for C/S testing before commencing antibiotics.

Statistical Analysis

Statistical analysis was done with the help of SPSS (standard version) program. For clinical features, a descriptive analysis was performed and results were presented as mean/standard deviation and percentages for quantitative and qualitative variables respectively. Moreover Chi square and t tests were used to find out the difference between qualitative and continuous data respectively. p - values of < 0.05 were considered to be statistically significant.

RESULTS

Mean age of the patients was 45.0 ± 25.0 years. There were 120 (60%) males and 80 (40%) females. Mean duration of CLD was 8.43 ± 1.37 months. Dominant part of the patients 114 (57%) had > 8 months of duration of CLD. Culture negative neutrocytic ascites was found in 118 (59%) patients. Comparison was done to see the effect of age, gender and duration of CLD on the outcome. Chi-square test was applied. Results were shown in below tables.

Table 1: Age of the Patients n = 200.

Mean ± SD	Minimum	Maximum
45 ± 25	20	70

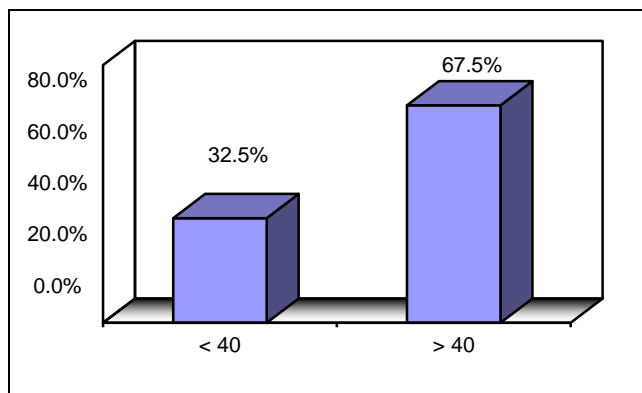


Figure 1: Age Group (in Years).

Table 2: Duration of CLD (in Months) n = 200.

Mean ± SD	Minimum	Maximum
8.43 ± 1.37	6	11

DISCUSSION

Patient with cirrhosis are at increased risk of many complications and have a decreased life expectancy. One of the main complications of cirrhosis with ascites is SBP and its prevalence is 6-30%.¹¹⁻¹²

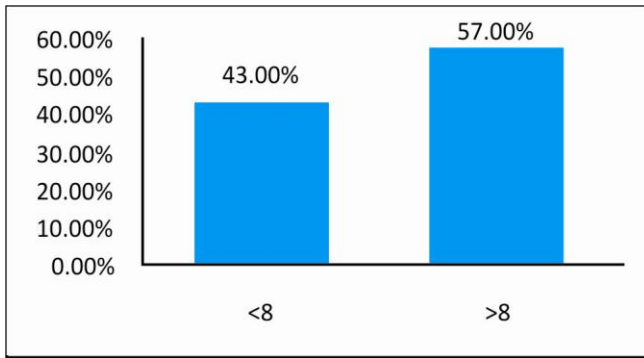


Figure 2: Duration of CLD (in Months).

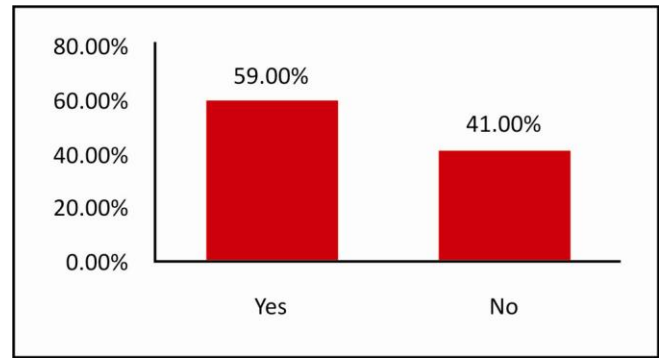


Figure 3: Culture Negative Neutrocytic Ascites.

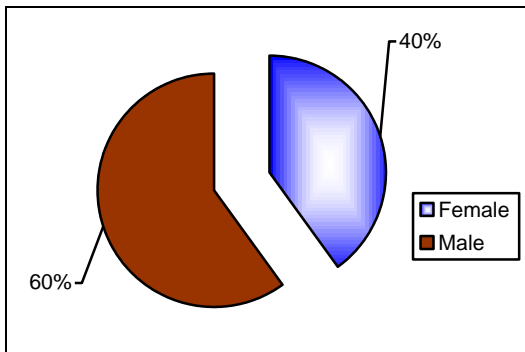


Figure 4: Gender Distribution.

In our study, culture negative neutrocytic ascites was found in 118 (59%) patients. In another study, among the cultured samples of presumed SBP, 123 (66.2%) presented negative cultures and 63 (33.8%) had positive results.¹³

In a local study on CLD patients the classical SBP was present in 50 (39.06%), Bacterascites in 6 (4.68%) and Culture Negative Neutrocytic Ascites (CNNA) in 72 (56.25%).¹⁴ In another local study 22 patients were found to have SBP among which 11 were culture negative and the remaining were culture positive.¹⁵

Among fifty patients, 28 (56%) were found to have SBP or its type, however classic SBP was found only in 11 (39.28%) patients, CNNA was present in 16 (57.14%) patients, one patient (3.57%) had bacterascites.¹⁶ In patients with cirrhosis SBP pathogenesis is thought to be the major consequence of bacteria translocation (BT). In bacterial translocation bacteria or their products enter into intestinal lumen and then pass in mesenteric lymph nodes or extra-intestinal area leading inflammatory reaction and ultimately infection. Moreover BT is also to be implicated in aggravating hemostasis disorders and hyperdynamic

Table 3: Comparison of Culture Negative Neutrocytic Ascites & Age n = 200.

Age (Years)	Culture-Negative Neutrocytic Ascites		Total	P-Value
	Yes	No		
≤40	38 (32.92%)	27 (32.92%)	65 (32.5%)	0.984
> 40	80 (67.80%)	55 (67.07)	135 (67.5%)	
Total	118 (100%)	82 (100%)	200 (100%)	

Table 4: Comparison of Culture Negative Neutrocytic Ascites & Gender distribution n = 200.

Duration of CLD (in Months)	Culture-Negative Neutrocytic Ascites		Total	P-Value
	Yes	No		
Male	70 (59.32%)	50 (60.97%)	120 (60%)	0.721
Female	48 (40.68%)	32 (39.02)	80 (40%)	
Total	118 (100%)	82 (100%)	200 (100%)	

Table 5: Culture-Negative Neutrocytic Ascites and Duration of CLD (in Months) n = 200.

Duration of CLD (in Months)	Culture-Negative Neutrocytic Ascites		Total	P-Value
	Yes	No		
< 8	47 (39.83%)	39 (47.56%)	86 (43%)	0.873
> 8	71 (60.17%)	43 (52.44)	114 (57%)	
Total	118 (100%)	82 (100%)	200 (100%)	

state. Proposed mechanisms being involved in BT in cirrhotic patients are structural and functional alterations in mucosal barriers, the deficiencies of local immune response and intestinal bacterial overgrowth. Intestinal bacterial overgrowth is considered to be the

main factors involved in BT. There are some other factors which seem to be causing decreased intestinal motility, sympathoadrenal stimulation, increased NO formation and the oxidative stress. Remember, normally there is significantly reduced microbial activity in small intestinal as compared to that of colon however this is reversed in cirrhotic patients.¹⁷

The clinical presentation of SBP is extremely variable, mostly present with fever pain abdomen and altered GI motility, others may have hepatic encephalopathy or renal failure, patients with SBP may be even asymptomatic so it is strongly recommended to perform diagnostic ascitic tap in all cirrhotic patients with ascites which has significantly reduced the episode of SBP.²

A similar prevalence of SBP (22%) in admitted patients had been reported by Amarapurkar DN et al.^{33,34} However the prevalence of SBP depends upon the extent of liver disease, it is considered to be higher in severe liver disease. The prevalence of SBP was 34.92% among 63 patient (of Child-Pugh Class C) reported by Jain et al. out of 63 patients. All patients who had SBP were in child class C.¹⁸ Out of 70 patients, 21 had SBP or its type and about 77% had Child-Pugh Class C reported by AS et al.¹⁸⁻¹⁹ In patients with de-compensated liver disease, triggering factor like SBP can lead to death. It is worth mentioning that physicians should have high index of suspicion and low threshold for diagnosis of SBP.^{18,20}

RECOMMENDATIONS

From our study it is concluded that Majority of the CLD patients presenting to tertiary care hospital have culture negative neutrocytic ascites so patient fulfilling the criteria of spontaneous bacterial peritonitis should be treated empirically without waiting for culture and sensitivity report. Cefotaxime is still drug of choice to treat SBP.

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